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EXAMINER	
SHEINBERG, MONIKA B	
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1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)
	09/856,333	BERLIN, KATHRIN
	Examiner	Art Unit
	Monika B Sheinberg	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-29* is/are rejected.

7)☒ Claim(s) *8,13 and 27* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *3 sheets* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action* .

DETAILED ACTION

Claims 1-29 are hereby examined.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

- Claims 1-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
  - Claim 1-5 and 18-24 are rejected as indefinite because the instantly claimed method lacks a final process step that clearly relates back to the preamble. For example, the method of claim 1, the preamble of the instantly claimed method is drawn to a method for the identification of 5-methylcytosine positions in genomic DNA yet the final process step is that of introducing a detectable label into the heteroduplex; no action of actual identification has occurred. The dependent claims 2-5 and 18-24 also do not have any active step of identifying the desired positions. Method claims require a last step or phrase in the last step that states the accomplishments of the goals for the method, which were stated in the method's preamble. Claim 1 lacks such a last step and is confusing because the additional method step is not sufficiently set forth in the claim or claims 2-5 and 18-24. While minute details are not required in method claims, at least the basic steps must be recited in a positive, active fashion. It is suggested that an amended claim more clearly describing the intended steps be submitted. As such claims 6-17 and 25-27 are also indefinite due to their dependency from claims 1-5 and 18-24.
  - Claim 1 is vague and indefinite due to the lack of clarity in the steps of methodology. The confusing methodology is unclear as to the order in which the method is to be performed in a stepwise manner in addition to what products or intermediaries occur and when. The following are some examples:
    - are the two products the nucleic-acid segments;

- are the nucleic-acid segments the same or two different segments just merely the same in region from which is selected from the genomic DNA (currently the term "the same" would indicate they are but one, however the segment of step b is from another cell therefore contradicting the term "same"); and
- at what point did the genomic DNA become a segment; is there a difference between the duplex in line 5 versus the heteroduplex of line 10.

Applicant is requested to utilize consistent terminology in the claim language; i.e. gene fragments, nucleic-acid segments, segment (alone), fragment (alone); in addition to differentiating between different segments. As such claims 2-27 are also indefinite due to dependency from claim 1.

- Claim 6 recites the limitation that "a 5-methylcytosine was localized in the genomic DNA" in lines 3-4. This lacks antecedent basis because the 5-methylcytosine was not localized, found or identified in any DNA of claim 1 (from which claim 6 depends) or claim 6. As such claims 9, 10 and 27 are also indefinite due to dependency from claim 6.
- Claims 7 and 8 recite the limitations that cytosine and 5-methylcytosine were found in the genomic DNA of claim 1 as seen for example in claim 7: "pairings occur at the positions at which cytosine was found in the genomic DNA" (lines 2-3). The claims lack antecedent basis because neither the cytosine nor the 5-methylcytosine were found or identified in any DNA of claim 1.
- Claim 8 is vague and indefinite due to the lack in clarity as to the further limitation of claim 1 by forming a heteroduplex with a demethylated reference DNA. The mismatch or erroneous base pairing that occurs in claim 8 already occurs in claim 1 in the formation of a heteroduplex with a reference DNA where in the mismatch in the formed heteroduplex indicates the location of a 5-methylcytosine. Thus it is unclear how claim 8 further limits claim 1.
- The term "sufficiently selective" in claim 9 is a relative term which renders the claim indefinite. The term "sufficiently" as well as "selectively" are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. In addition the phrase itself is confusing in that the terms seems to contradict each other.

- The term "sufficiently selectively" in claim 10 is a relative term which renders the claim indefinite. The term "sufficiently" as well as "selectively" are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. In addition the phrase itself is confusing in that the terms seems to contradict each other.
- Claim 11 is vague and indefinite due to the lack of clarity in the claim language "that DNA fragments are obtained in step e) according to claim 1" lines 1-2. The phrase is confusing because step e) of claim 1 merely introduces a label and no DNA fragments are obtained. As such claims 12-17 are also indefinite due to dependency from claim 11.
- Claim 15 is vague and indefinite due to the lack of clarity in the claim language "the size of the fragments produced in step e) according to claim 1" lines 1-2. The phrase is confusing because step e) of claim 1 merely introduces a label and no DNA fragments are produced. As such claims 16 and 17 are also indefinite due to dependency from claim 15.
- Claim 16 is vague and indefinite due to the lack of clarity in term "introduced" line 2. It is unclear as to what are the metes and bounds of the parameters that define "introduced" in the context of the "several PCRs of a gene segment". As such claim 17 is also indefinite due to dependency from claim 16.
- Claims 16 and 17 are vague and indefinite due to the lack of clarity in the claim language "set stepwise newly each time" (claim 16, line 2) and "positioned newly stepwise" (claim 17, line 2). The language does not make sense thus making it unclear as to what is intended by the Applicant.
- Claim 18 is vague and indefinite due to the lack of clarity in the term "chemical function" line 2. It is unclear as to what are the metes and bounds of the parameters that define "chemical function". It is unclear what further limitation has been provided to the primer such as the ability to be further chemical modification, or further modification for binding to another substrate that allows immobilization, or immediate immobilization.
- Claim 25 is vague and indefinite due to the lack of clarity in the term "one" line 1. It is unclear what "one" is referring to.
- Claim 26 is vague and indefinite due to the lack of clarity in the steps of methodology.

> Method according to claim 1, further characterized in that a preselection of gene segments to be investigated in detail by the mass spectrometer is conducted by means of fluorescence labeling of the immobilized DNA strand, the lack of which, after conducting steps d) and e) of claim 1 and a washing step, indicates the presence of methylated cytosines in the investigated genomic DNA.

The claim language does not follow in a stepwise manner that clearly depicts that which Applicant intends for the steps of the method. For example, lines 2-3 (of above) recite the labeling of "the immobilized DNA strand" yet nowhere in the claim 26 or claim 1 (from which claim 26 depends) has a strand of DNA been immobilized; in addition it is unclear as to which DNA strand is to be immobilized, the genomic DNA, fragment, segment, etc. The claim continues to recite "the lack of which, after conducting steps d) and e) of claim 1 and a washing step" is confusing as to what is being referred to in "the lack of which". The DNAs within the body of the claim are also confusing as to which is which and at what point: preselected gene segments versus the immobilized DNA strand versus the investigated DNA. Applicant is requested to use consistent terminology to maintain clear and definite claim language.

- Claim 27 is vague and indefinite due to the lack of clarity of the term "preselection" line 2. The metes and bounds of the parameters required for preselecting a gene segment are unclear.
- Claim 27 is vague and indefinite due to the lack of clarity of the term "a more non-specific variant" line 3. It is unclear as to what are the metes and bounds of the parameters that define a "variant", one that is a "non-specific variant", or one that is "more non-specific"; and to what degree is it "more" non-specific.
- Regarding claim 27, the word "means" (line 2), it is unclear if the use of the term is an attempt to use a "means" clause to recite a claim element as a means for performing a specified function. If such was intended, then it is necessary for the words which precede "means" to convey a function to be performed. However, currently no function is specified by the word(s) preceding "means," it is impossible to determine the equivalents of the element.
- The following claims 1, 11, 12, 15-20 and 26-28 lack antecedent basis for the indicated limitations in the claims:
  - Claim 1 recites the limitations "the identification", "the two products", "the duplex", "the same nucleic-acid segment", "the at-least two amplified products" in lines 1, 5, 6, 8 and 10 respectively.
  - Claim 11 recites the limitation "the cleavage positions" in line 2.

- Claim 12 recites the limitation "the analysis" in line 1.
- Claim 15 recites the limitation "the fragments" in line 2.
- Claim 16 recites the limitation "the primers" in line 2.
- Claim 17 recites the limitation "the PCR primers" and "the other primer" in lines 1-2 and 3 respectively.
- Claims 18-20 recites the limitations "the PCR" and "the PCR products".
- Claim 26 recites the limitations "the mass spectrometer" and "the immobilized DNA strand" in lines 6 and 7.
- Claim 27 recites the limitation "the gene segments" in line 2.
- Claim 28 recites the limitation "the variable methylation positions" in line 3.

As such, claims 2-10, 13, 14, 21-25, and 29 are also indefinite due to dependency from claims 1, 11, 12, 15 and 28.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

- Claims 1-3, 4, 5, 6, 9-11, 19-25, 28 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,750,335 (Gifford, May 12, 1998) in view of US Patent 6,017,704 (Herman et al.).

Gifford demonstrates a method of identifying nucleotide variations through a genetic screening method that involves:

> Hybridizing a "test, i.e., a potential variant, nucleic acid, e.g., from a patient, with a nucleic acid standard. If the test and the standard (reference) nucleic acids contain one or more nucleotide sequence differences, then the double stranded nucleic acid formed from hybridization of the sequences will contain one or more nucleotide pair mismatches, i.e., will comprise a heteroduplex. In accordance with the invention, protocols are provided which permit detection of the presence of the heteroduplex [...and the] detection [...] methods involve exploitation of the selective binding properties of mismatch binding proteins." (column 3, lines 40-55)

In addition, Figure 10 further demonstrates the amplification of the test and reference DNA by a polymerase reaction wherein the amplified products are heteroduplexes. Therefore as shown above and in Figure 10, Gifford demonstrates the method steps of performing an amplification reaction on a test DNA which has a single point mutation (such as a 5-methlycytosine) and a reference DNA [claim 1 steps (a)-(c)] followed by the formation of heteroduplexes with mismatches between the test and reference DNA [claim 1 step (d)] and heteroduplex mismatch detection by mismatch specific labeling [claim 1 step (e)]. [With respect to 1(a) chemical treatment, please see further below]. Gifford demonstrates the applicability of the described method to mismatches "such as asymmetric methylation, can be detected with proteins that bind to hemi-methylated nucleic acids" (column 28, lines 64-66) as required by the instant claims for identifying methylation patterns in genomic DNA (claim 1, preamble). The reference teaches DNA "may be genomic DNA, cDNA, MRNA, synthetic polynucleotide, mitochondrial DNA, amplified or circular DNA, or other single or double stranded polynucleotide, from whatever source" (column 4, lines 49-54) for the use in the described method in identifying genetic mutations [claim 1 (a), source of DNA]. Further the reference demonstrates a "labeled form of the mismatch protein"(column 5, lines15-16), such as MutS (column 7, lines 14-25) as required by claims 1 (step e) and 21-23 in which the enzyme that forms a complex to the non-complementary base pair (claim 21) is MutS (claim 22) and bears a label allowing the complex to be displayed (claim 23). The protein bound label as required by claim 24 is demonstrated to be a fluorescent antibody (columns 15-16, bridging sentence). Claims 2 and 25 are demonstrated by the reference in the comparison of the reference nucleic acid to numerous test nucleic acids (column 15 lines 60-67; also column 5, lines 1-12) which as stated above can be "from whatever source" thus a comparison of different nucleic acids from a variety of sources such as different cells or different individuals result in different or variable methylation positions and/or patterns. The joint labeling (claim 5) of multiple samples after heteroduplex formation is demonstrated in column 5 (lines 1-30) wherein multiple samples form heteroduplexes upon a spot array followed by labeling the resulting mismatches with a detectable label introduced to the heteroduplex by a mismatch binding protein. Gifford teaches the transfer of the amplified products (claims 19 and 20) to different vessels (affinity columns or affinity matrix) for purification of the heteroduplexes wherein the products are coupled to a solid support (column 5, lines 47-56).

- With respect to claims 6 and 9-11, although the method demonstrated by Gifford does not specifically include the limitations of erroneous base pairings equal methylation position (claim 6), "chemical mismatch cleavage" (claim 9), enzymatic cleavage (claim 10), and DNA fragment size from cleavage indicates methylation positions (claim 11); the reference demonstrates the state of the art being well known at the time the instant application was filed. The limitations of claims 6, 9 and 10 are well known in the art as stated by Gifford that the creation and detection of a heteroduplex molecule (mismatched base pairs) between a test and reference DNA are performed (claim emphasis added) "by ribonuclease cleavage [claim 10] of mismatched pyrimidine bases of RNA/DNA hybrids and detection of point of cleavage in the molecule; [...] and chemical modification and cleavage of mismatched bases using hydroxylamine (to modify cytosine) [claim 6] or osmium tetroxide (to modify thymidine) modification and peperidine cleavage [claim 9], and subsequent detection of cleaved DNA" (column 1, lines 38-59). Gifford further states it is well known in the art to use RFLP analysis (columns 1-2, bridging paragraph) for the "subsequent detection of cleaved DNA" which was cleaved specifically at points of non-complementary base pairing (claim 11). Due to the chemical treatment of specific bases of DNA to created non-complementary base pairing as required by claim 1 step (a) being well known in the prior art, it would have been obvious for one of ordinary skill in the art to analyze methylated genomic DNA as per the method of Gifford to identify positions of 5-methylcytosine.
- With respect to claim 1, step (a) in the chemical treatment of the cytosine and 5-methylcytosine for altering base pair behavior; and claim 3, the chemical treatment being a bisulfite treatment, Gifford does not teach these limitations.

Herman et al. teaches the process of chemically treating cytosine (without altering 5-methylcytosine) by a bisulfite reaction method in order to identify methylated cytosines (column 6, lines 24-35).

Thus, it would have been *prima facia* obvious to one of ordinary skill in the art at the time of the invention was made to perform the genetic mutation detection and identification method of Gifford and further modify treatment of genomic DNA to include chemical medications such as the bisulfite reaction as per the teachings of Herman et al. One of ordinary skill in the art would have been motivated to include chemical modification for the method of identifying methlated cytosines because Herman et al. specifically utilizes the method step for

detection of methylated and non-methylated nucleic acids. In addition the required chemical treatment of specific bases of DNA to created non-complementary base pairing is well known in the prior art as stated by Gifford (column 1, lines 38-59) for the purpose of detecting altered base pair behavior.

- With respect to claims 28 and 29, Gifford does not teach kits that include (un)methylated DNA and corresponding reagents for identification of methylated cytosines.

Herman et al teaches kits for the identification of methylated cytosines that include methylated and unmethylated genomic DNA and reagents necessary for the chemical modifications (bisulfite reaction) of the DNA (column 18 line 60 - column 19, line 15).

Thus, it would have been *prima facia* obvious to one of ordinary skill in the art at the time of the invention was made to perform the genetic mutation detection and identification method of Gifford and further modify the kits for performing methylation detection to include the reagents for DNA chemical treatment and methylation as per the teachings of Herman et al. One of ordinary skill in the art would have been motivated modify the kits of Gifford (column 6, lines 51-64) to include reagents for methylation and (un)methylated DNA as required by claims 28 and 29 for completion of the described method for methylation mutation identification as suggest by Gifford (column 28, lines 64-66).

- With respect to claim 4, the joint amplification of genomic DNA of several samples, would be obvious for one of ordinary skill in the art to perform due to the practice of amplifying multiple samples jointly being a common within the laboratory setting for the expected benefit of achieving increased efficiency through multiplexing amplifcation reactions.

- Claims 12-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,750,335 (Gifford, May 12, 1998) in view of US Patent 6,017,704 (Herman et al.) as applied to claims 1-3, 5, 6, 9-11, 19-25, 28 and 29 above; and further in view of WO 97/33000 (Monforte et al., 12-Sept-1997).

The teachings of Gifford and Herman et al. are set forth above.

Monforte et al. demonstrates a method of identifying positions of general base pair mismatch mutations by mass spectrometry (claim 12), specifically by means of matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF) and electrospray

ionization mass spectrometry (ESI) as required by claims 13 and 14 (p. 19, lines 18-24). The optimization of the DNA fragment size for optimal mass spectrometry results as required by claims 15-17 is demonstrated on page 24 (lines 13-20):

> Typically, the target nucleic acid would be amplified by a number of DNA amplifications, - 10-20, in order to reduce the number of fragments to be analyzed in any given sample. Each amplified target nucleic acid product would be digested using restriction endonucleases, often with four-base recognition sites to produce the optimal size fragments.

(Note that as the claims fail to set forth clear and definite optimization steps in claims 16 and 17 and due to the above results of varied fragment size being the same as in the instant claims for mass spectrometry optimization, claims 16 and 17 are encompassed by the method demonstrated by Monforte et al.) .

Thus, it would have been *prima facia* obvious to one of ordinary skill in the art at the time of the invention was made to perform the genetic mutation detection and identification method of Gifford and further modify the method and kit to include treatment of genomic DNA by chemical medications such as the bisulfite reaction and as per the teachings of Herman et al. (as described above). It would have further been *prima facia* obvious to one of ordinary skill in the art at the time of the invention was made include the mass spectrometry analysis as per the teachings of Monforte et al. The ordinary artisan would have been motivated modify the method of Gifford in view of Herman et al. to use mass spectrometry in the mutation identification method as taught by Monforte et al. for the purpose of improving the method for the "extremely detailed information about the molecules being analyzed including high mass accuracy" and it's easy automation (p. 6, lines 3-6). Further, on page 36 Monforte et al. clearly describes utilizing the basic method of identifying mismatch mutation postions in heteroduplexes in a hybrid formed from a wildtype and mutant sequences using chemical treated and amplified DNA by mass spectrometry as required by claim 1. Monforte et al. demonstrates the analysis of heteroduplexes, or heterozygous hybrids, wherein a base pair mismatch on the DNA fragments are specifically located by mass spectrometry as a result of size (molecular weight) analysis (claim 12) and cleavage positions are indicative of the type of mutation (claim 11):

> With this heterozygous hybrid, it is possible to use one of the structure-specific enzymes or chemistries described in the following section to create a mutation-specific cleavage at the site of a mutation. An example of the pattern of nonrandom length fragments produced is

> shown in FIG. 9. This approach permits determination of the type and location of the mutation that has occurred. (p. 36, lines 24-28)

In addition, the above structure-specific enzymatic or chemistries for mutation-specific cleavage are demonstrated by pages 4-5 in methods of enzymatic mismatch cleavage and chemical mismatch cleavage as required by claims 9 and 10. Furthermore Monforte et al. demonstrates the improved ability of identifying mismatches created by chemically modifying cytosines to uracils (claim 13) by mass spectrometry because "[n]ormally the masses of C and U vary by only 1 Da, making it practically impossible to detect C to U or U to C point mutations within a given fragment"(pp. 27-28, bridging paragraph). Therefore the ordinary artisan would have had a reasonable expectation of success that the method of using mass spectrometry as taught by Monforte et al. would be useful in the method of Gifford in view of Herman et al., because Monforte et al. demonstrates the identifying the position base pair mismatch mutations in a general fashion that encompasses the required chemical treatment to alter specific base pairs, formation of heteroduplexes, and mass spectrometry as required by the instant claims.

Claim Objections

Claim 8 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of claim 1. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 13 is objected to due to the improper abbreviation applied to a matrix-assisted laser desorption/ionization time-of-flight mass spectrometry. Currently the claim recites "MALDI" whereas the appropriate abbreviation is "MALDI-TOF".

Claim 27 objected to because of the following informalities: the instant claim is improperly dependent from claims 1-25; claims 27 must claim dependency from claims 1-25 in the alternative, for example "any one of claims 1-25". Appropriate correction is required.

Specification

The disclosure is objected to because of the following informality: The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC (See 37 CFR 1.52(e)(5) and MPEP 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text are permitted to be submitted on compact discs.) or
REFERENCE TO A "MICROFICHE APPENDIX" (See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.)
(e) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(f) BRIEF SUMMARY OF THE INVENTION.
(g) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(h) DETAILED DESCRIPTION OF THE INVENTION.
(i) CLAIM OR CLAIMS (commencing on a separate sheet).
(j) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(k) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

Conclusion

- Claims 1-29 are rejected under 35 U.S.C. 112, second paragraph.
- Claims 1-3, 4, 5, 6, 9-11, 19-25, 28 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,750,335 (Gifford) in view of US Patent 6,017,704 (Herman et al.).
- Claims 12-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,750,335 (Gifford) in view of US Patent 6,017,704 (Herman et al.); and further in view of WO 97/33000 (Monforte).
- Claims 8, 13 and 27 are objected.

- Objection to the specification.

No claim is allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Monika B. Sheinberg, whose telephone number is (703) 306-0511. The examiner can normally be reached on Monday-Friday from 9 A.M to 5 P.M. If attempts to reach the examiner by telephone are unsuccessful, the primary examiner in charge of the prosecution of this case, Jehanne Souaya, can be reached at 703-308-6565. If attempts to reach the examiners are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst, Chantae Dessau, whose telephone number is (703) 605-1237, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

October 1, 2003
Monika B. Sheinberg
Art Unit 1634

Jehanne Souaya
JEHANNE SOUAYA
PATENT EXAMINER
Primary
10/1/03